16 September 2008

This supplement has been prepared to present scientific and technical news items that may be of more interest to technical personnel at RDT&E activities and the labs, or the medics rather than the broader readership of the basic CB Daily. Due to the nature of the material, the articles, if available online, are usually only available through subscription services thus making specific links generally unavailable. Thus, usually only the bibliographic citation is available for use by an activity's technical library.

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Chem-Bio News – Pandemic Influenza Supplement #27

1. ANTIVIRAL RESEARCH (PROGRESS IN IDENTIFYING VIRULENCE DETERMINANTS OF THE 1918 H1N1 AND THE SOUTHEAST ASIAN H5N1 INFLUENZA A VIRUSES:
"Defining how individual viral proteins promote enhanced replication, inflammation and severe disease will provide insight into the pathogenesis of severe influenza virus infections and suggest novel therapeutic approaches."

2. DROSOPHILA RNAI SCREEN IDENTIFIES HOST GENES IMPORTANT FOR INFLUENZA VIRUS REPLICATION: *"This could accelerate the development of new classes of antiviral drugs for chemoprophylaxis and treatment, which are urgently needed given the obstacles to rapid development of an effective vaccine against pandemic influenza and the probable emergence of strains resistant to available drugs."*

3. A SEVEN-SEGMENTED INFLUENZA A VIRUS EXPRESSING THE INFLUENZA C VIRUS GLYCOPROTEIN HEF: *"These results support a selective mechanism of viral RNA recruitment to the budding site."*

4. COMPARATIVE EFFICACY OF NEUTRALIZING ANTIBODIES ELICITED BY RECOMBINANT HEMAGGLUTININ PROTEINS FROM AVIAN H5N1 INFLUENZA VIRUS: *"Taken together, these results suggest that recombinant HA proteins as individual or oligomeric trimers can elicit potent neutralizing antibody responses to avian H5N1 influenza viruses."*

5. BODY EXHUMED IN FIGHT AGAINST FLU: *"The body of an aristocrat who died nearly 90 years ago has been exhumed in the hope that it will help scientists combat a future flu pandemic."*

CB Daily Report

ANTIVIRAL RESEARCH (PROGRESS IN IDENTIFYING VIRULENCE DETERMINANTS OF THE 1918 H1N1 AND THE SOUTHEAST ASIAN H5N1 INFLUENZA A VIRUSES
Drug Week
September 19, 2008

"The 1918 pandemic H1N1 influenza virus and the recently emerged Southeast Asian H5N1 avian influenza virus are unique among influenza A virus isolates in their high virulence for humans and their lethality for a variety of animal species without prior adaptation. Reverse genetic studies have implicated several viral genes as virulence determinants."

"For both the 1918 and H5N1 viruses, the hemagglutinin and the polymerase complex contribute to high virulence. Non-structural proteins NS1 and PB1-F2, which block host antiviral responses, also influence pathogenesis. Additionally, recent studies correlate high levels of viral replication and induction of strong proinflammatory responses with the high virulence of these viruses."

"Defining how individual viral proteins promote enhanced replication, inflammation and severe disease will provide insight into the pathogenesis of severe influenza virus infections and suggest novel therapeutic approaches."

The full article can be found at: (C.F. Basler, et. al., “Progress in identifying virulence determinants of the 1918 H1N1 and the Southeast Asian H5N1 influenza A viruses”. Antiviral Research, 2008;79(3):166-78). Link not available.

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DROSOPHILA RNAI SCREEN IDENTIFIES HOST GENES IMPORTANT FOR INFLUENZA VIRUS REPLICATION
Genomics & Genetics Weekly
September 19, 2008

"Here we describe a novel genome-wide RNA interference (RNAi) screen in Drosophila 1 that can be used to identify host genes important for influenza virus replication. After modifying influenza virus to allow infection of Drosophila cells and detection of influenza virus gene expression, we tested an RNAi library against 13,071 genes (90% of the Drosophila genome), identifying over 100 for which suppression in Drosophila cells significantly inhibited or stimulated reporter gene (Renilla luciferase) expression from an influenza-virus-derived vector. The relevance of these findings to influenza virus infection of mammalian cells is illustrated for a subset of the Drosophila genes identified; that is, for three implicated Drosophila genes, the corresponding human homologues ATP6V0D1, COX6A1 and NXF1 are shown to have key functions in the replication of H5N1 and H1N1 influenza A viruses, but not vesicular stomatitis virus or vaccinia virus, in human HEK 293 cells. Thus, we have demonstrated the feasibility of using genome-wide RNAi screens in Drosophila to identify previously unrecognized host proteins that are required for influenza virus replication."

"This could accelerate the development of new classes of antiviral drugs for chemoprophylaxis and treatment, which are urgently needed given the obstacles to rapid development of an effective vaccine against pandemic influenza and the probable emergence of strains resistant to available drugs."

The full article can be found at: (L.H. Hao, et. al., “Drosophila RNAi screen identifies host genes important for influenza virus replication”. Nature, 2008;454(7206):890-U46). Link not available.

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A SEVEN-SEGMENTED INFLUENZA A VIRUS EXPRESSING THE INFLUENZA C VIRUS GLYCOPROTEIN HEF

Medical Devices & Surgical Technology Week
September 21, 2008

"Influenza viruses are classified into three types: A, B, and C. The genomes of A- and B-type influenza viruses consist of eight RNA segments, whereas influenza C viruses only have seven RNAs. Both A and B influenza viruses contain two major surface glycoproteins: the hemagglutinin (HA) and the neuraminidase (NA)."

"Influenza C viruses have only one major surface glycoprotein, HEF (hemagglutinin-esterase fusion). By using reverse genetics, we generated two seven-segmented chimeric influenza viruses. Each possesses six RNA segments from influenza virus A/Puerto Rico/8/34 (PB2, PB1, PA, NP, M, and NS); the seventh RNA segment encodes either the influenza virus C/ Johannesburg/1/66 HEF full-length protein or a chimeric protein HEF-Ecto, which consists of the HEF ectodomain and the HA transmembrane and cytoplasmic regions. To facilitate packaging of the heterologous segment, both the HEF and HEF-Ecto coding regions are flanked by HA packaging sequences. When introduced as an eighth segment with the NA packaging sequences, both viruses are able to stably express a green fluorescent protein (GFP) gene, indicating a potential use for these viruses as vaccine vectors to carry foreign antigens. Finally, we show that incorporation of a GFP RNA segment enhances the growth of seven-segmented viruses, indicating that efficient influenza A viral RNA packaging requires the presence of eight RNA segments."

"These results support a selective mechanism of viral RNA recruitment to the budding site."

The full article can be found at: (Q.S. Gao, et. al., “A seven-segmented influenza A virus expressing the influenza C virus glycoprotein HEF”. Journal of Virology, 2008;82(13):6419-6426). Link not available.

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COMPARATIVE EFFICACY OF NEUTRALIZING ANTIBODIES ELICITED BY

RECOMBINANT HEMAGGLUTININ PROTEINS FROM AVIAN H5N1 INFLUENZA VIRUS
Health & Medicine Week
September 15, 2008

"Although the human transmission of avian H5N1 virus remains low, the prevalence of this highly pathogenic infection in avian species underscores the need for a preventive vaccine that can be made without eggs. Here, we systematically analyze various forms of recombinant hemagglutinin (HA) protein for their potential efficacy as vaccines."

"Monomeric, trimeric, and oligomeric H5N1 RA proteins were expressed and purified from either insect or mammalian cells. The immunogenicity of different recombinant HA proteins was evaluated by measuring the neutralizing antibody response. Neutralizing antibodies to H5N1 HA were readily generated in mice immunized with the recombinant HA proteins, but they varied in potency depending on their multimeric nature and cell source. Among the HA proteins, a high-molecular-weight oligomer elicited the strongest antibody response, followed by the trimer; the monomer showed minimal efficacy. The coexpression of another viral surface protein, neuraminidase, did not affect the immunogenicity of the HA oligomer, as expected from the immunogenicity of trimers produced from insect cells. As anticipated, HA expressed in mammalian cells without NA retained the terminal sialic acid residues and failed to bind alpha 2,3-linked sialic acid receptors."

The researchers concluded: "Taken together, these results suggest that recombinant HA proteins as individual or oligomeric trimers can elicit potent neutralizing antibody responses to avian H5N1 influenza viruses."

The full article can be found at: (C.J. Wei, et. al., “Comparative efficacy of neutralizing antibodies elicited by recombinant hemagglutinin proteins from avian H5N1 influenza virus”. Journal of Virology, 2008;82(13):6200-6208). Link not available.

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BODY EXHUMED IN FIGHT AGAINST FLU
BBC
September 16, 2008

“The body of an aristocrat who died nearly 90 years ago has been exhumed in the hope that it will help scientists combat a future flu pandemic.

Yorkshire landowner Sir Mark Sykes died in France in 1919 from Spanish flu.

Sir Mark was buried in a lead coffin which scientists hope may have helped preserve the virus.

They believe his remains will help piece together the DNA of Spanish flu, which could have a similar genetic structure to modern bird flu.”

The full article can be found at: http://news.bbc.co.uk/1/hi/england/humber/7617968.stm

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